PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: R. Sanders WILLIAMS *et al.*	Group Art Unit: 1653
Serial No.: 09/782,953	Examiner: Liu, Samuel W.
Filed: February 13, 2001	Atty. Dkt. No.: MYOG:036US/SLH
For: METHODS AND COMPOSITIONS RELATING TO MUSCLE SELECTIVE CALCINEURIN INTERACTING PROTEIN (MCIP)	

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37 C.F.R. §1.8

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October 6, 2005
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Steven L. Highlander

APPEAL BRIEF

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Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-01450

Dear Sir:

This brief is filed (in triplicate) in response to the Final Office Action mailed on April 20, 2005, regarding the above-captioned application. This brief is due on October 22, 2005, by virtue of the Notice of Appeal received by the PTO July 22, 2005; the enclosed Petition for Extension of Time. The fee for the brief was paid on September 20, 2005 and this filing supersedes the Appeal Brief filed on September 20, 3005. Should any other fees be due, or should appellants' check be missing, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.:50-1212/MYOG:036US/SLH. Please date stamp and return the attached postcard as evidence of receipt.

I. Status of the Claims

Claims 1-101 were filed with the application. Claims 1-58, 60, 63-69 and 71-101 have been canceled. Thus, claims 59, 61, 62, and 70 are pending, stand rejected, and are appealed. A copy of the pending claims is attached.

II. Status of the Amendments

There are no amendments at this time

III. Statement of Interest

The real party in interest is the assignee, The Board of Regents, University of Texas System. Myogen, Inc. is the exclusive licensee of the application.

IV. Related Appeals and Interferences

There are no related appeals or interferences.

V. Summary of the Invention

The present invention is drawn to methods of modulating muscle cell growth comprising (a) providing a modulator of MCIP expression; and (b) administering a modulator to a subject, whereby administration of said modulator results in modulation of muscle cell growth. Specification at page 6, lines 24-27, and page 7, lines 1-13.

VI. Issues on Appeal

Are claims 59, 61, 62 and 70 indefinite under 35 U.S.C. §112, second paragraph?

Are claims 59, 61, 62 and 70 obvious under 35 U.S.C. §103?

VII. Grouping of the Claims

The claims stand or fall together.

VIII. Summary of the Argument

The rejections under §112, second paragraph, are based on the premise that generic claims that covers both up- and down-regulation of muscle cell growth are indefinite. This is not the case. The claims clearly set forth that an agent is provided to a subject, and that said agent may either increase (agonist) or decrease (antagonist) the growth of muscle cells in the subject. Whatever other issues might be raised by these claims, clarity cannot reasonably be challenged. Moreover, the use of the term "second pharmaceutical composition" in claim 70 is not indefinite, and in any event, appellants have previously offered an amendment to claim 59 that would resolve the issue but it was not accepted.

The obviousness rejection is improper because it is an attempt to use an inherency-type argument in an obviousness context. The claims specifically read on inhibitors of MCIP. The examiner relies on references that disclose inhibitors of Calcineurin, an upstream mediator of MCIP, to make the invention obvious. These references published before it was ever known that MCIP was downstream of Calcineurin in the molecular cascade leading to cardiac hypertrophy and heart failure. The examiner has thus relied on references that do not disclose all the claimed elements of the invention, and in fact, published before the relationship between MCIP and Calcineurin was known. Thus, the examiner cannot properly refer to these articles to support an obviousness rejection when the very nature of obviousness requires an ability of one of skill in the art to infer the invention from the references, and such an inference is not possible in this case.

IX. Argument

A. Standard of Review

Findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. §706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Rejection Under 35 U.S.C. §112, Second Paragraph

The examiner has repeatedly rejected claims 59, 61, 62 and 70 under the second paragraph of §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter. The examiner continues to argue that the claims are indefinite in the use of the term "modulation" as not defining whether the regulation is up or down. This objection clearly is improper, as explained in detail below.

The very essence of the present claims is to identify molecules that may modify MCIP expression ***in either direction – up or down***; hence the use of the word ***modulation***, which is generic to up- or down-regulation, accurately reflects the intent of the claim, and is thus very much correct in its usage. By way of example, the Merriam-Webster dictionary defines

modulate as to "vary" or "adjust" or "alter" and does not describe a direction in which such variation or adjustment occurs. The specification does not dispute or redefine this meaning. A modulator is thus, by definition, something that is capable of varying something else, and a modulator of MCIP expression can therefore vary the expression of MCIP in any direction, up or down. There is nothing indefinite about this recitation, and reversal of this rejection is respectfully requested.

In the Final Office Action, the examiner once again defends his reasoning by arguing that a modulator cannot be both an agonist and an antagonist, and hence claims the recitations in claims 61 and 62, respectfully, are also unclear. Nothing could be further from the truth. Claims 61 and 62 are dependent claims. Thus, they further limit the subject matter of claim 59, which as already pointed out, is generic with respect to the direction of regulation. There is absolutely nothing indefinite about these claims either. Reversal of this rejection is respectfully requested as well.

Claim 70 is also rejected over the term "second pharmaceutical agent." Appellants previously amended claim 70 to clarify that the second pharmaceutical agent is distinct from the agent provided in claim 59. Appellants attempted to amend claim 59 to specify a first pharmaceutical agent (*i.e.*, the modulator), in that claim, but entry of this amendment was denied. Appellants are more than willing to provide an additional amendment, or authorize the examiner to make such an amendment. Even if this amendment is not entered, however, appellants submit that one of skill in the art would recognize that the "second pharmaceutical agent" of claim 70 is in addition to the modulator of claim 59, and thus there is no issue of indefiniteness. Reversal of this rejection is respectfully requested.

C. Rejection Under 35 U.S.C. §103

Claims 59, 61, 62 and 70 are rejected under 35 U.S.C. §103(a) as allegedly being obvious in light of Chin *et al.*, and Sussman *et al.* The examiner asserts that these references, which teach the modulation of muscle cell growth through the inhibition of calcineurin, make obvious the claims of modulating MCIP to modulate muscle cell growth, since MCIP was later found to be both activated by and capable of modulating the activity of calcineurin. Both the Chin and Sussman references teach modulation of skeletal muscle or cardiac muscle by inhibiting calcineurin, yet neither reference mentions or discloses MCIP or its relation to or interaction with calcineurin. Furthermore, neither reference discloses methods practiced in humans, although Sussman makes a suggestion to do so (which is at best an invitation to experiment by suggesting that administration of cyclosporin could be beneficial in the setting of some heart and muscle diseases). The examiner alleges that it would have been a "mechanistic extrapolation" to go from the teachings of Chin (which shows that inhibition of calcineurin can modulate muscle cell growth in an animal) to the current invention. He further alleges that the suggestion by Sussman cited above somehow makes obvious the concept of modulating MCIP in human disease.

Applicants contend, as stated in the prior responses, that in order to make modulation of MCIP obvious in light of these references, the examiner is improperly relying on inherency in the context of an obviousness rejection and is not applying a valid obviousness analysis to the two cited references. Since MCIP's relation to calcineurin was not known at the time these references published, a person of ordinary skill in the art could not have foreseen that link and then attempted to modulate MCIP to modulate muscle cell growth. Until that link was discovered, the prior art gave no guidance to one of skill that attempting to modulate MCIP would do anything to muscle cell growth.

The proper analysis of references that are used to support an obviousness rejection should focus on whether the references would render the invention obvious based on the knowledge that one of skill in the art would gain from the references, not based on what is later discovered to be true. The fact that a specific result or pathway might flow inherently from the practice of a process or discovery of a partial biological pathway is immaterial if the skilled artisan "would not appreciate or recognize that inherent result." *In re Naylor*, 152 USPQ 106 (CCPA 1966). Furthermore, *In re Spormann*, 150 USPQ 449 (CCPA 1966) says that "the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." That statement describes the current situation since both of the cited references existed before the knowledge of MCIP's role in cardiac biology was fully elucidated. The fact that it was later discovered that calcineurin could modulate MCIP would not and could not make it obvious to one of skill in the art, prior to that discovery, that modulating MCIP could be accomplished by modulating calcineurin. In other words, since MCIP's relationship to calcineurin was "unknown" at the time these references published, they cannot be used as "predicates" for an obviousness rejection.

Perhaps even more to the point, neither reference renders obvious the steps of (i) selecting a human patient or (ii) selecting a modulator of MCIP with which to treat that human patient, both of which are affirmative recitations in the instant claims, for the simple reason that neither step is taught or suggested by the references. Thus, the examiner has simply ignored required elements of the claims, relying instead on the flawed inherency argument to support an obviousness rejection. As stated above, this is not proper. In light of these statements, reconsideration and reversal of these rejections is respectfully requested.

X. Conclusion

In light of the foregoing, appellants respectfully submit that all pending claims are definite and supported by the application as filed. Therefore, it is respectfully requested that the Board reverse each of the pending rejections.

Respectfully submitted,

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CLAIMS APPENDIX

1-58. (Canceled)

59. (Previously presented) A method of modulating muscle cell growth in a human subject comprising:

(a) identifying a human subject in need of muscle cell growth modulation;
(b) selecting a small molecule modulator of MCIP1 expression; and
(b) administering said modulator to said human subject,

whereby administration of said modulator results in modulation of muscle cell growth in said subject.

60. (Canceled)

61. (Previously presented) The method of claim 59, wherein said small molecule modulator is an agonist of muscle cell growth.

62. (Previously presented) The method of claim 59, wherein said small molecule is an antagonist of muscle cell growth.

63-69. (Canceled)

70. (Previously presented) The method of claim 59, further comprising administering to said human subject a second pharmaceutical agent used to treat cardiac disease.

71-101. (Canceled)

CITED AUTHORITIES APPENDIX

Administrative Procedure Act, 5 U.S.C. §706(A), (E), 1994
Dickinson v. Zurko, 527 U.S. 150, 158 (1999)
In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000)
In re Naylor, 152 USPQ 106 (CCPA 1966)
In re Spormann, 150 USPQ 449 (CCPA 1966)

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

None